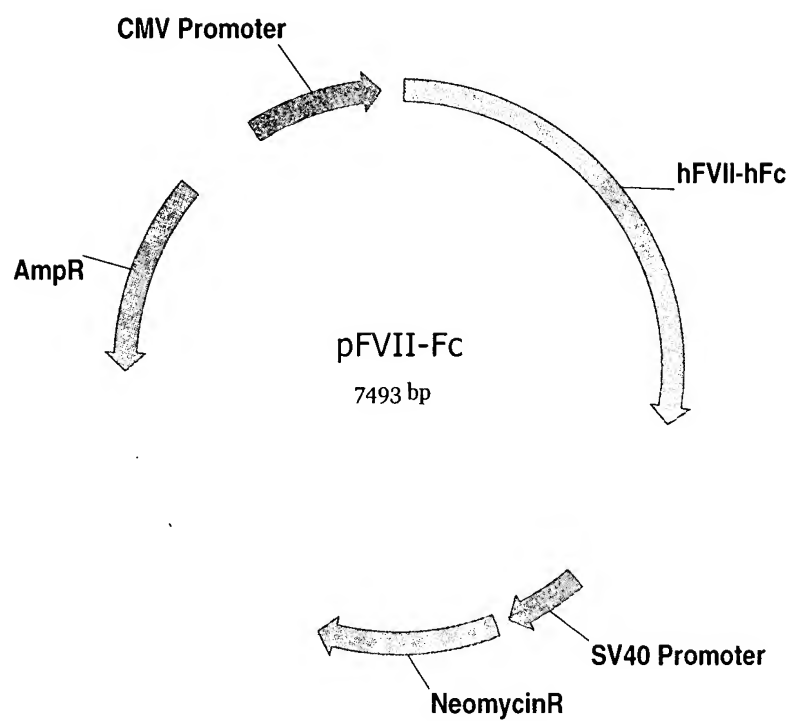


FIGURE 1 – Plasmid vector pFVII-Fc according to example 1

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53

2/9

FIGURE 2

SEQ ID NO:1 (The amino acid sequence of native human coagulation Factor VII):

5
Ala-Asn-Ala-Phe-Leu-GLA-GLA-Leu-Arg-Pro-Gly-Ser-Leu-GLA-Arg-GLA-Cys-Lys-
5 10 15
GLA-GLA-Gln-Cys-Ser-Phe-GLA-GLA-Ala-Arg-GLA-Ile-Phe-Lys-Asp-Ala-GLA-Arg-
10 20 25 30 35
Thr-Lys-Leu-Phe-Trp-Ile-Ser-Tyr-Ser-Asp-Gly-Asp-Gln-Cys-Ala-Ser-Ser-Pro-
40 45 50
15 Cys-Gln-Asn-Gly-Gly-Ser-Cys-Lys-Asp-Gln-Leu-Gln-Ser-Tyr-Ile-Cys-Phe-Cys-
55 60 65 70
Leu-Pro-Ala-Phe-Glu-Gly-Arg-Asn-Cys-Glu-Thr-His-Lys-Asp-Asp-Gln-Leu-Ile-
75 80 85 90
20 Cys-Val-Asn-Glu-Asn-Gly-Gly-Cys-Glu-Gln-Tyr-Cys-Ser-Asp-His-Thr-Gly-Thr-
95 100 105
Lys-Arg-Ser-Cys-Arg-Cys-His-Glu-Gly-Tyr-Ser-Leu-Leu-Ala-Asp-Gly-Val-Ser-
25 110 115 120 125
Cys-Thr-Pro-Thr-Val-Glu-Tyr-Pro-Cys-Gly-Lys-Ile-Pro-Ile-Leu-Glu-Lys-Arg-
130 135 140
30 Asn-Ala-Ser-Lys-Pro-Gln-Gly-Arg-Ile-Val-Gly-Gly-Lys-Val-Cys-Pro-Lys-Gly-
145 150 155 160
Glu-Cys-Pro-Trp-Gln-Val-Leu-Leu-Leu-Val-Asn-Gly-Ala-Gln-Leu-Cys-Gly-Gly-
165 170 175 180
35 Thr-Leu-Ile-Asn-Thr-Ile-Trp-Val-Val-Ser-Ala-Ala-His-Cys-Phe-Asp-Lys-Ile-
185 190 195

54

3/9

Lys-Asn-Trp-Arg-Asn-Leu-Ile-Ala-Val-Leu-Gly-Glu-His-Asp-Leu-Ser-Glu-His-
200 205 210 215

5 Asp-Gly-Asp-Glu-Gln-Ser-Arg-Arg-Val-Ala-Gln-Val-Ile-Ile-Pro-Ser-Thr-Tyr-
220 225 230

Val-Pro-Gly-Thr-Thr-Asn-His-Asp-Ile-Ala-Leu-Leu-Arg-Leu-His-Gln-Pro-Val-
235 240 245 250

10 Val-Leu-Thr-Asp-His-Val-Val-Pro-Leu-Cys-Leu-Pro-Glu-Arg-Thr-Phe-Ser-Glu-
255 260 265 270

Arg-Thr-Leu-Ala-Phe-Val-Arg-Phe-Ser-Leu-Val-Ser-Gly-Trp-Gly-Gln-Leu-Leu-
15 275 280 285

Asp-Arg-Gly-Ala-Thr-Ala-Leu-Glu-Leu-Met-Val-Leu-Asn-Val-Pro-Arg-Leu-Met-
290 295 300 305 306

20 Thr-Gln-Asp-Cys-Leu-Gln-Gln-Ser-Arg-Lys-Val-Gly-Asp-Ser-Pro-Asn-Ile-Thr-
310 315 320

Glu-Tyr-Met-Phe-Cys-Ala-Gly-Tyr-Ser-Asp-Gly-Ser-Lys-Asp-Ser-Cys-Lys-Gly-
325 330 335 340

25 Asp-Ser-Gly-Gly-Pro-His-Ala-Thr-His-Tyr-Arg-Gly-Thr-Trp-Tyr-Leu-Thr-Gly-
345 350 355 360

Ile-Val-Ser-Trp-Gly-Gln-Gly-Cys-Ala-Thr-Val-Gly-His-Phe-Gly-Val-Tyr-Thr-
30 365 370 375

Arg-Val-Ser-Gln-Tyr-Ile-Glu-Trp-Leu-Gln-Lys-Leu-Met-Arg-Ser-Glu-Pro-Arg-
380 385 390 395

35 Pro-Gly-Val-Leu-Leu-Arg-Ala-Pro-Phe-Pro
400 405 406

55

4/9

SEQ ID NO:2 (DNA primer 1 for preparation of hFVII-hFc):

5'- GCTAGCCACCATGGTCTCCCAGGCCCTCAG -3' (SEQ ID NO:2)

5 SEQ ID NO:3 (DNA primer 2 for preparation of hFVII-hFc):

5'- CGAGCCCCATTTCCCGGATCCGCAGAGCCCAAATCTTGT -3' (SEQ ID NO:3)

SEQ ID NO:4 (DNA primer 3 for preparation of hFVII-hFc):

5'- CGAGCCCCATTTCCCGGATCCGCAGAGCCCAAATCTTGT -3' (SEQ ID NO:4)

10

SEQ ID NO:5 (DNA primer 4 for preparation of hFVII-hFc):

5'- TTGCCGGCCGTCGCACTCATTTA -3' (SEQ ID NO:5)

15 SEQ ID NO:6 (The amino acid sequence of native human coagulation Factor VII with alternative spliced propeptide (underlined) conjugated to Fc domain of IgG1, native human coagulation Factor VII underlined. :

MVSQALRLLCLLLGLQGCLAAGGVAKASGGETRDMPWKPGPHRVFVTQEEAHGVLHRRRRANAF
LEELRPGSLERECKEEQCSFEEAREIFKDAERTKLFWISYSDGDQCASSPCQNGGCKDQLQSYICF
20 CLPAFEGRNCETHKDDQLICVNENGGCEQYCSHTGTGRSCRHEGYSLADGVSTPTVEYPCGKI
PILEKRNASKPQGRIVGGKVC PKGEC PWQVLLLVNGAQLCGGTLINTIWVVSAAHCFDKIKNWRNLIA
VLGEHDLSEHDGDEQSRRVAQVIIPSTYVPGTTNHDIALRLHQPVVLTDHVVPLCLPERTFSERTLAF
VRFSVLVSGWGQLDRGATALELMVLNVPRMTQDCLQQSRKVG DSPNITEYMFCAGYSDGSKDSCK
GDSGGPHATHYRG TWYLTGIVSWGQGCATVGHFGVYTRVSQYIEWLQKLMRSEPRPGVLLRAPFP
25 GSAEPKCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYV
DGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREP
QVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDK
SRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

30

SEQ ID NO:7 (Amino acid sequence of Fc domain from IgG1):

EPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGV
EVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVY
35

TLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPVLDSGDSFFLYSKLTVDKSR
WQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

5

SEQ ID NO:8 (The amino acid sequence of native human coagulation Factor VII conjugated to Fc domain of IgG1, native human coagulation Factor VII underlined, X refers to GLA residues):

10 ANAFLLXLRPGSLXRXCKXXQCSFXXARXIFKDAXRTKLFWISYSDGDQCASSPCQNGGSCCKDQLQS
YICFCLPAFEGRNCETHKDDQLICVNEGGCEQYCSDHTGTRSCRCHEGYSLLADGVSCTPTVEYP
CGKIPILEKRNASKPQGRIVGGKVCPKGECPWQVLLLVNGAQLCGGTLINTIWVVSAAHCFDKIKNWR
NLIAVLGEHDLSEHDGDEQSRRVAQVIPSTYVPGTTNHDIALRLHQPVVLTDHVVPLCLPERTFSE
RLAFVRFSLVSGWGQLDRGATALELMVLNVPRLMTQDCLQQSRKVGDSPNITEYMFCAGYSDGSK
15 DSCKGDSGGPHATHRGTWYLTGIVSWGQGCATVGHFGVYTRVSQIEWLQKLMRSEPRPGVLLR
APFPGSAEPKSCDKTHTCPPCAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVDVSHEDPEVKFN
WYVDGVEVHNAKTKPREEQNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKQP
REPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDSGSFFLYSKLT
VDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

20

SEQ ID NO:9 (cDNA sequence encoding the amino acid sequence of native human coagulation Factor VII with alternative spliced propeptide conjugated to Fc domain of IgG1:

atggtctcccaggccctcaggctcctctgccttctgcttggcctcagggtgcctggctcaggcgggctgctaaggcctcaggaggagaaa
cacgggacatgccgtggaagccggggcctcacagagcttctgtaaccaggaggaagcccacggcgctcctgcacccggcgccggcgccg
25 aacggcttctggaggagctgcggccgggctccctggagagggagtgcaaggaggagcagtgctccttcgaggaggcccgaggatcttc
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gaccagctccagctctatactgcttctgcctccctgcctcagggccggaactgtgagcgcacaaggatgaccagctgactgtgtgaacg
agaacggcggtgtgagcagtgactgcagtgaccacacgggcaccaagcgctcctgtcggtgccagaggggtactctctgtgagcagcgg
30 ggtgtcctgcacaccacagttgaatatccatgtggaaaaatactattctagaaaaaagaaatgccagcaaaccccaaggccgaattgtg
ggggcaagggtgtccccaaaggggagtgatgagcaggtcctgtgtgtggaatggagctcagttgtgtggggggaccctgatcaacacca
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cagccccatcgagaaaacctctccaaagccaaagggcagccccgagaaccacaggtgtacacctgccccatcccggtgagctg
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aacaactacaagaccacgctcccgtgctggactccgacggctccttctctacagcaagctcacggtggacaagagcaggtggcagca
ggggaacgttctcatgctccgtgatgcatgaggctcgcacaaccactacacgcagaagagccttccctgtctccgggtaaatga

5

SEQ ID NO:10 (cDNA sequence encoding the vector comprising the cDNA sequence encoding the amino acid sequence of native human coagulation Factor VII with alternative spliced propeptide conjugated to Fc domain of IgG1:

gtagaccacatggtctcccaggccctcaggctcctctgcttctggttgcagggtcctggctgcaggcggggtcgctaaggcctcag
10 gaggagaaacacgggacatgccgtggaagccggggcctcacaagctctcgtacccaggaggaagcccacggcgtcctgcacggcg
ccggcgcgccaacgcgttcttgaggagctcggccgggctccctggagaggagtgcaaggaggagcagtgctcctcgaaggggcc
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gctcctgcaaggaccagctccagtcctatctgcttctgctccctgcttgcaggggccgaactgtgagacgcacaaggatgaccagctgat
15 ctgtgtgaacgagaacggcggtgtgagcagctactgcagtgaccacacgggcaccaagcgctcctgtcgggtgccacgaggggtactctgc
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35 catgctggggatgcggtgggctctatggctctgaggcggaagaaccagctggggctctaggggtatccccacggccctgtagcggcgc
attaagcggcggggtgtgtgtgtacgcgcagcgtgaccgtacactgccagcgccctagcggccgctccttctccttctccttctcgt
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ttaggtgatgttgcagtagtgggccatcgccctgatagacggttttgcctttagcgttgaggtccagcttcttaatagtgagctgttccaa
actggaacaacactcaaccctatctcggtctattctttagttataagggttttccgatttccgctattggttaaaaatgagctgatttaaaaa
40 aatttaacgcgaattattctgtggaatgtgtgtagttaggtgtggaagtccccaggctccccagcaggcagaagtatgcaaaagcatgcat
ctcaattagtcagcaaccagggtgtggaagtccccaggctccccagcaggcagaagtatgcaaaagcatgcatctcaattagtcagcaaccat
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55 acaataaagcaatagcatcacaatttcacaaataaagcatttttactgcattctagttgtgttgcacaaactcatcaatgtatctatcatgtc

7/9

5 tgtataccgtcgacctctagctagagcttggcgtaatacatggtcatagctgttctgtgtaaatgttatccgctcacaattccacacacatacga
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 25 cgtggtgtcacgctcgtcgttggatggtcattcagctccggttcccaacgatcaaggcgagttacatgatccccatgttgcagaaaaagcg
 gttagctccttcggtctccgatcgttgcagaagtaagttggccgagtggtatcactcatggttatggcagcactgcataattcttactgtcatgc
 catccgtaagatgctttctgtgactggtgagtaactcaaccaagtcattctgagaatagtgatgcggcgaccgagttgctctgccggcgctcaat
 acgggataataaccgcgcatagcagaactttaaaagtgtcatcattgaaaaacgttcttcggggcgaaaaactcgaagatcttaccgctg
 ttgagatccagttcgtatgaaccactcgtgcacccaactgatcttcagcatctttactttcaccagcgtttctgggtgagcaaaaacaggaaggc
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 gatcgggagatctcccgatccctatggtgcactctcagtaacaatctgctctgatgccgcatagttaagccagtatctgctccctgctgtgtgtg
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 35 atatatggagttccggttacataactacggtaaatggccgcctggctgaccgcccacgacccccgccattgacgtcaataatgacgtat
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 acatctacgtattagtcgtctattaccatggtgatgcggttttggcagtaacatgggctggttagcggtttagctcacggggatttccaagt
 ctccacccattgacgtcaatgggagttgtttggcaccaaaaacacgggactttccaaaatgtcgttaacaactccgccccattgacgcaaat
 gggcggtaggcgtgtacggtgggaggtctatataagcagagctcttggttaactagagaacccactgcttactggcttatcgaaattaatc
 40 actcactatagggagaccaagctg

SEQ ID NO:11 (The amino acid sequence of native human coagulation Factor VII with propeptide (underlined) conjugated to Fc domain of IgG1, native human coagulation Factor VII underlined. Construct is made according to example 1):

40 MVSQALRLCLLLGLQGCLAAVFVTQEEAHGVLHRRRRANAFLEELRPGSLERECKEEQCSFEAR
EIFKDAERTKLFWISYSDGDQCASSPCQNGGCKDQLQSYICFLPAFEGRNCETHKDDQLICVNN
GGCEQYCSDHTGTRKSCRCHEGYSLLADGVSCTPTVEYPCGKIPILEKRNASKPQGRIVGGKVCPKG
ECPWQVLLLVNGAQLCGGTLINTIWVVSAAHCFDKIKNWRNLIAVLGEHDLSEHDGDEQSRRVAQVII
 45 PSTYVPGTTNHDIALLRLHQPVVLDHVVPLCLPERTFSERTLAFVRFSLVSGWGQLLDRGATALELM
VLNVPRLMTQDCLQQSRKVGDSPNITEYMFCAGYSDSSKDSCKGDSGGPHATHYRGTWYLTGIVS
WGQGCATVGHFGVYTRVSQYIEWLQKLMRSEPRPGVLLRAPFPGSAEPKSCDKTHTCPPCPAPPELL
GGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRV
 50 VSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVK
GFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHY
TQKSLSLSPGK

SEQ ID NO:12 (cDNA sequence encoding the amino acid sequence of native human coagulation Factor VII with propeptide conjugated to Fc domain of IgG1, cDNA construct is made according to example 1):

8/9

atggctcccaggccctcaggctcctctgcttctgcttgggttcagggtgcttgcagctctcgttaaccaggaggaagcccacggcgtc
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gtctccgggtaaatga

25

SEQ ID NO:13 (cDNA sequence encoding the vector comprising the cDNA sequence encod-
ing the amino acid sequence of native human coagulation Factor VII with propeptide conju-
gated to Fc domain of IgG1, cDNA construct is made according to example 1):

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[illegible]